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EXAMINER	
FERNANDEZ, KATHERINE L	
ART UNIT	**PAPER NUMBER**
3768	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,116	GRINVALD ET AL.	
	Examiner	Art Unit	
	Katherine L. Fernandez	3768	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/1/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Priority

1. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Claim Objections

2. Claim 83 is objected to because of the following informalities:

Claim 83 makes reference to Claim 38 which has been previously canceled by applicant. Examiner assumes that claim 83 is dependent on claim 82.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 45-46 are rejected under 35 U.S.C. 102(e) as being anticipated by Flower et al. (US Patent No. 6,351,663).

With regards to claim 45, Flower et al. disclose a method for vascular analysis of a subject, comprising the steps of optically imaging at least one optically accessible blood vessel of a subject (column 2, lines 46-67; column 7, line 50 – column 8, lines 5; column 8, lines 19-34); determining from said optical imaging at least one flow characteristic of erythrocytes in said at least one optically accessible blood vessel

(column 2, lines 59-67, referring to determining the direction of the blood flow in the blood vessel; column 6, lines 22-48); and utilizing said at least one flow characteristic for determining the roughness on said inner wall of said at least one optically accessible blood vessel (column 3, lines 1-17, referring to analyzing angiographic images (i.e. analyzing blood flow) to determine whether a lesion is present in the wall of a body cavity (i.e. indicator of roughness on inner wall)).

With regards to claims 46-48, the optically accessible blood vessel can be a retinal blood vessel, located in tissue of an internal organ, or the tissue can be selected from gastro-intestinal tissue, brain tissue and the internal surface of a passageway (column 10, lines 53-56).

With regards to claim 49, detecting the presence of roughness on the inner wall of a blood vessel of a subject is performed non-invasively (column 3, lines 4-17, referring to detecting the presence of roughness on the inner wall by analyzing angiographic image, which is performed non-invasively).

With regards to claim 50, at least two sequential images of erythrocytes in the blood vessel are acquired (column 2, lines 59-67; column 9, line 65 through column 10, lines 7, referring to angiograms being obtained at selected time intervals).

5. Claims 59-63 are rejected under 35 U.S.C. 102(e) as being anticipated by Strauss (US Patent No. 6,782,289).

With regards to claims 59-62, Strauss discloses a method for detecting arteriosclerotic plaque on the walls of blood vessels of a subject, comprising the steps of: providing a biochemical label for said plaque having predetermined optical properties

(column 2, line 64 through column 3, line 23; column 4, lines 31-45, referring to the use of visible markers such as fluorescent labels); labeling of at least part of said arteriosclerotic plaque with said biochemical label (column 2, line 64 through column 3, line 23); and optically imaging at least one optically accessible blood vessel to detect said labeled arteriosclerotic plaque (column 5, lines 43-56; column 7, lines 41-49). The optical accessible blood vessel can be an esophageal blood vessel (column 7, lines 12-26). Further, they disclose that the biochemical label can be fluorescent and can be an antibody label (column 4, line 31-column 5, line 10).

With regards to claims 63-65, Strauss discloses a method for detecting arteriosclerotic plaque on the walls of blood vessels of a subject, comprising the steps of: providing a radioactive biochemical label for said arteriosclerotic plaque (column 4, lines 11-30); labeling at least part of said arteriosclerotic plaque with said radioactive biochemical label (column 2, line 64 through column 3, line 23); and radiographically imaging at least one of said blood vessels of the subject to detect said radioactively-labeled arteriosclerotic plaque (column 5, lines 43-56; column 7, lines 41-49). Regarding claim 64, some blood vessels may not be optically accessible (column 3, lines 49-67).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flower et al. in view of Wong et al. as cited by applicant ("Retinal microvascular abnormalities and incident stroke: the Atherscleroses Risk in Communities Study", October 2001).

As discussed above, Flower et al. meet the limitations of claim 45. However, they do not specifically disclose that the step of determining the roughness on the inner wall of the blood vessel is utilized in order to ascertain the condition of another blood vessel of the subject, or that the roughness on the inner wall of the blood vessel is utilized to ascertain the level of arteriosclerosis in the subject. Wong et al. disclose a study investigating the relation between retinal microvascular abnormalities to incident stroke (pg. 1134, left column, Summary:Background). They conclude that retinal microvascular lesions (i.e. roughness on wall of blood vessel) can be markers of general vascular pathology (such as atherosclerosis, which is a form of arteriosclerosis) rather than specific microvascular pathology (pg. 1139, left column, 1st paragraph). At the time of the invention, it would have been obvious to one of ordinary skill in the art to have included the above limitations to the method of Flower et al.. The motivation for doing so would have been to provide a non-invasive way to be able to determine the risk of arteriosclerosis in an individual, as taught by Wong et al. (pg. 1139, left column, 1st paragraph).

8. Claims 53, 66-67, 70-77 and 79-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flower et al. in view of Taylor et al. ("Finite Element Modeling of

Three-Dimensional Pulsatile Flow in the Abdominal Aorta: Relevance to Atherosclerosis", 1998) .

With regards to claim 53 and 70, Flower et al. do not specifically disclose that at least one flow characteristic of said erythrocytes comprises at least one of the mean curvature of the motion lines of said erythrocytes, the deviation from cylindrical symmetry of the motion lines of said erythrocytes, the spatial density of local turbulences in the motion lines of said erythrocytes, and the local deviations from the global character of the motion lines of said erythrocytes. Taylor et al. disclose a study investigating detailed quantitative data on hemodynamic conditions in the abdominal aorta (Abstract). They disclose that their method involves obtaining velocity field maps in order to study pulsatile flow in the abdominal aorta, and analyzing flow characteristics of the velocity field, such as observing that the velocity field in the infrarenal abdominal aorta is directed preferentially towards the anterior wall (pg. 983-986, Section: Discussion). At the time of the invention, it would have been obvious to one of ordinary skill in the art to have the flow characteristic in the method of Flower et al. to comprise at least one of the characteristics discussed above. The motivation for doing so would have been to be able to provide correlations between findings and observed patterns of vascular disease, as taught by Taylor et al. (pg. 983, left column, 2nd paragraph).

With regards to claims 66-67 and 79-81, Flower et al. disclose a system for vascular analysis of a subject, comprising (i) a light source for illuminating at least one optically accessible blood vessel of the subject (column 7, lines 50-57) and (ii) an imager for acquiring a plurality of images showing sequential spatial distribution of

moving erythrocytes in said at least one optically accessible blood vessel (column 8, lines 19-34). Flower et al. further disclose utilizing a flow characteristic for determining the roughness on said inner wall of said at least one optically accessible blood vessel (column 3, lines 1-17, referring to analyzing angiographic images (i.e. analyzing blood flow) to determine whether a lesion is present in the wall of a body cavity (i.e. indicator of roughness on inner wall)). The optically accessible blood vessel can be a retinal blood vessel, located in tissue of an internal organ, or the tissue can be selected from gastro-intestinal tissue, brain tissue and the internal surface of a passageway (column 10, lines 53-56). However, they do not specifically disclose an image discriminator determining from said plurality of images showing sequential spatial distribution, a flow pattern of erythrocytes along said blood vessel, a flow analyzer analyzing said flow pattern to determine at least one flow characteristic of erythrocytes along said at least one optically accessible blood vessel of the subject; and a wall analyzer utilizing at least one flow characteristic for determining at least one property of the inner surface of said blood vessel. Taylor et al. disclose a computer with software designed to perform flow computations that can serve as an image discriminator, a flow analyzer, and a wall analyzer (pg. 979, left column, paragraphs 3-4). At the time of the invention, it would have been obvious to one of ordinary skill in the art to include the elements listed above in the system of Flower et al. The motivation for doing so would have been to be able to provide correlations between findings of flow characteristics and observed patterns of vascular disease, as taught by Taylor et al. (pg. 983, left column, 2nd paragraph).

With regards to claims 71-74, Flower et al. in view of Taylor et al. do not specifically disclose that their system further comprises a wavelength selecting device, such that said imager acquires said images of said at least one optically accessible blood vessel over a limited wavelength band, and wherein said wavelength selector is located in the illuminating pathway between said light source and said at least one optically accessible blood vessel or is located in the imaging pathway between said at least one optically accessible blood vessel and said imager. They also do not disclose that the wavelength band is between 2 and 30 nm. However, Flower et al. disclose that radiation wavelength is selected to excite a dye used in their method, and further that an endoscope may be used to obtain the images, and that an instrument would be used with the endoscope to provide radiation at an appropriate wavelength to cause the dye within the subject vessels to fluoresce (column 5, lines 3-19; column 8, lines 19-34). At the time of the invention, it would have been obvious to one of ordinary skill in the art to include the above discussed wavelength selecting device and have a wavelength band between 2 and 30 nm. The motivation for doing so would have been to be able to apply the appropriate wavelength to cause the dye to fluoresce, as taught by Flower et al. (column 8, lines 19-34).

With regards to claims 75-77, Flower et al. disclose the use of a pulsed laser (column 7, lines 50-54). Although they do not specifically disclose that the pulse interval is less than 1 second, between 5 and 200 milliseconds, or between 5 and 40 milliseconds, they do disclose that the advantage of pulsing the laser is that it provides a greater number of photons for image formation in the shortest time interval (column 7,

lines 50-54). At the time of the invention, it would have bee obvious to have the pulse interval be in the discussed ranges above. The motivation for doing so would have been to be able to have a greater number of photons for image formation in the shortest time interval, as taught by Flower et al. (column 7, lines 50-54)

9. Claims 54-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flower et al. in view of Taylor '02 ("In Vivo Quantification of Blood Flow and Wall Shear Stress in the Human Abdominal Aorta During Lower Limb Exercise", March 2002).

Flower et al. disclose a method for vascular analysis of a subject, comprising the steps of: (i) optically imaging at least one optically accessible blood vessel of a subject ((column 2, lines 46-67; column 7, line 50 – column 8, lines 5; column 8, lines 19-34); (ii) optically imaging said at least one optically accessible blood vessel again (column 10, lines 46-50, referring to obtaining a series of images); (iii) determining from said optical imaging of steps (i) and (ii) at least one flow characteristic of erythrocytes in said at least one optically accessible blood vessel (column 2, lines 59-67, referring to determining the direction of the blood flow in the blood vessel; column 6, lines 22-48); and (iv) utilizing differences obtained in said at least one flow characteristic to determine a roughness index of said inner wall of said at least one optically accessible blood vessel (column 3, lines 1-17, referring to analyzing angiographic images (i.e. analyzing blood flow) to determine whether a lesion is present in the wall of a body cavity (i.e. indicator of roughness on inner wall)). However, they do not disclose that step(i) is performed with subject having a first blood pressure, said blood pressure being subject to change,

that step (ii) is performed when said blood pressure of said subject has changed to a second value, nor do they disclose that the change from said first blood pressure to said second blood pressure is caused by at least one of exercise and drugs administered to the subject. They also do not disclose that the change of said first blood pressure to said second blood pressure is a result of the subject's heartbeat. Further, they do not disclose that their method also comprises of the step of synchronizing the optical imaging steps to the subject's heartbeat, and that the synchronizing is performed by monitoring at least one of the subject's heartbeat cycle and blood pressure, and using said monitoring to control the timing of the optical imaging.

Taylor '02 disclose a study that measures, in vivo, the spatial distribution of blood flow velocities in the abdominal aorta of human subjects during upright rest and light exercise conditions (pg. 403, left column, 3rd paragraph). They disclose that data was collected at rest and during steady-state exercise conditions within the range of light exercises (i.e. data was collected at two different heart rates, which cause a change in blood pressure; also scans were synchronized with the subject's heart beat) (pg. 403, right column, 2nd paragraph). Further, the subjects monitored their own heart rate, which was displayed in real-time on a pulse monitor (pg. 403, right column, 2nd paragraph). At the time of the invention, it would have been obvious to one of ordinary skill in the art to have step (i) and step(ii) in the method of Flower at al. be performed at different blood pressure readings. The motivation for doing so would have been to be able to determine the effect of activities that change blood pressure (such as exercise)

on flow characteristics, as taught by Taylor '02 (pg. 403, left column, 2nd-3rd paragraphs).

10. Claims 68-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Flower in view of Taylor '98 as applied to claims 53 and 66-67 above, and further in view of Wong et al.

Flower et al. in view of Taylor '98 do not specifically disclose an arteriosclerotic index determiner utilizing said roughness to determine the level of arteriosclerosis in said at least one optically accessible blood vessel, nor that the determiner utilizes said roughness to ascertain the arteriosclerotic condition of another blood vessel of the subject. Wong et al. disclose a study investigating the relation between retinal microvascular abnormalities to incident stroke (pg. 1134, left column, Summary:Background). They conclude that retinal microvascular lesions (i.e. roughness on wall of blood vessel) can be markers of general vascular pathology (such as atherosclerosis, which is a form of arteriosclerosis) rather than specific microvascular pathology (pg. 1139, left column, 1st paragraph). At the time of the invention, it would have been obvious to one of ordinary skill in the art to have the computer of Flower et al. in view of Taylor '98 perform as an arteriosclerotic index determiner as well. The motivation for doing so would have been to provide a non-invasive and effective way to be able to determine the risk of arteriosclerosis in an individual, as taught by Wong et al. (pg. 1139, left column, 1st paragraph).

11. Claim 78 rejected under 35 U.S.C. 103(a) as being unpatentable over Flower et al. in view of Taylor '98 as applied to claims 53, 66-67, and 70-77 above, and further in view of Flower '94 (US Patent No. 5,279,298).

As discussed above, Flower et al. in view of Taylor '98 meets the limitations of claim 66. However, they do not specifically disclose that the light source for illuminating the blood vessel of the subject imager is a continuous source, and said imager acquires images at predetermined intervals. Flower '94 discloses a method and apparatus to detect and treat neovascular membranes in the ocular vasculature of the fundus of the eye (column 1, lines 8-10). They disclose the use of a continuous light source and that the imager acquires the images at predetermined intervals (column 5, lines 34-52, referring to the computer recording successive images or frames of the fundus of the eye with the passage of time). At the time of the invention, it would have been obvious to one of ordinary skill in the art to include the above limitations in the system of Flower et al. in view of Taylor '98. The motivation for doing so would have been to be able to obtain an image when the maximum dye fluorescence occurs as taught by Flower '94 (column 6, lines 3-13).

12. Claims 82-83 and 85-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strauss in view of Leone et al. (US Patent No. 5,811,814).

Strauss discloses a system for vascular analysis of a subject comprising (i) a light source for illuminating at least one optically accessible blood vessel of the subject, after ingestion by the subject of a biochemical label which labels arteriosclerotic plaque such that it ahs predetermined optical properties (column 2, line 64-column 3, line 23;

column 5, line 43-56; column 7, lines 41-49); and an optical imager (or a radiographic apparatus) for acquiring at least one image of said at least one optically accessible blood vessel of the subject (column 7, lines 11-44). Further, they disclose that the biochemical label can be fluorescent and can be an antibody label (column 4, line 31-column 5, line 10). Regarding claim 87, some blood vessels may not be optically accessible (column 3, lines 49-67). However, they do not specifically disclose that their system further includes an image processor to determine the amount and location of regions of said predetermined optical properties of said arteriosclerotic plaque and a mapper to generate a map of the arteriosclerotic deposits in the walls of said at least one optically accessible blood vessel of the subject (i.e. a plaque location deriver utilizing at least one image provided by apparatus to determine the location of the radioactive biochemical label). Leone et al. disclose an apparatus and method for measuring radiation levels in a region of interest in a body of a subject (column 1, lines 6-12). They disclose that their system includes a radiation detecting assembly and a radiation measurement assembly (column 4, lines 28-37). The detected radiation is converted to a relative measure of radiation by the radiation measurement assembly, which includes an output display device (column 5, lines 1-12; column 7, line 62 – column 8, line 5). Hot spots of high radiation can be viewed on a fluoroscopy screen (i.e. mapping of hot spots) (column 5, lines 13-21). At the time of the invention, it would have been obvious to one of ordinary skill in the art to include an image processor and a mapper in the system of Strauss. The motivation for doing so would have been to

provide precise determination of the damaged or diseased area of the blood vessel for the physician, as taught by Leone et al. (column 2, lines 45-50).

13. Claim 84 is rejected under 35 U.S.C. 103(a) as being unpatentable over Strauss in view of Leone as applied to claims 82-83 and 85-88 above, and further in view of Wong et al.

Strauss in view of Leone do not specifically disclose that the map of arteriosclerotic deposits in the walls of the blood vessel of the subject is utilized to ascertain the arteriosclerotic condition of another blood vessel of the subject. Wong et al. disclose that retinal microvascular lesions (i.e. roughness on wall of blood vessel) can be markers of general vascular pathology (such as atherosclerosis, which is a form of arteriosclerosis) rather than specific microvascular pathology (pg. 1139, left column, 1st paragraph). At the time of the invention, it would have been obvious to one of ordinary skill in the art to have the map of arteriosclerotic deposits be utilized to ascertain the arteriosclerotic condition of another blood vessel of the subject. The motivation for doing so would have been to provide a non-invasive way to be able to determine the risk of arteriosclerosis in an individual, as taught by Wong et al. (pg. 1139, left column, 1st paragraph).

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine L. Fernandez whose telephone number is (571)272-1957. The examiner can normally be reached on 8:30-5, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eleni M. Mantis-Mercader can be reached on (571)272-4740. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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